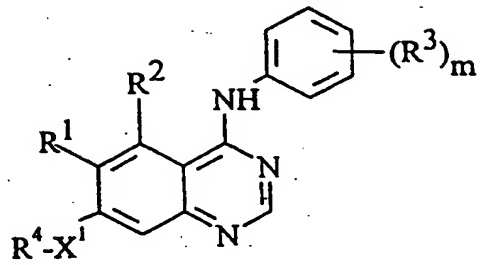
CLAIMS

1. A quinazoline derivative of the formula I:



(I)

[wherein:

m is an integer from 1 to 2;

R^1 represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkylthio, or $-NR^5R^6$ (wherein R^5 and R^6, which may be the same or different, each represents hydrogen or C_{1-3}alkyl);

R^2 represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro;

R^3 represents hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

X^1 represents -O-, $-CH_2-$, -S-, -SO-, $-SO_2-$, $-NR^7CO-$, $-CONR^8-$, $-SO_2NR^9-$, $-NR^{10}SO_2-$ or $-NR^{11}-$ (wherein R^7, R^8, R^9, R^{10} and R^{11} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);

R^4 is selected from one of the following thirteen groups:

1) C_{1-5}alkylR^{12} (wherein R^{12} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C_{1-5}alkyl through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) or C_{1-5}alkylR^{13} (wherein R^{13} is a group selected from pyrrolidin-1-yl, imidazolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-}

$_4$alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

2) C_{2-5}alkenylR^{14} (wherein R^{14} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

3) C_{2-5}alkynylR^{15} (wherein R^{15} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

4) C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16} (wherein X^2 and X^3 which may be the same or different are each -O-, -S-, -SO-, $-SO_2-$, $-NR^{17}CO-$, $-CONR^{18}-$, $-SO_2NR^{19}-$, $-NR^{20}SO_2-$ or $-NR^{21}-$ (wherein R^{17}, R^{18}, R^{19}, R^{20} and R^{21} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{16} represents hydrogen or C_{1-3}alkyl) with the proviso that X^1 cannot be $-CH_2-$ when R^4 is C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16};

5) C_{1-5}alkylX^4COR^{22} (wherein X^4 represents -O- or $-NR^{23}-$ (wherein R^{23} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{22} represents $-NR^{24}R^{25}$ or $-OR^{26}$ (wherein R^{24}, R^{25} and R^{26} which may be the same or different each represents hydrogen, C_{1-4}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

6) C_{1-5}alkylX^5R^{27} (wherein X^5 represents -O-, -S-, -SO-, $-SO_2-$, -OCO-, $-NR^{28}CO-$, $-CONR^{29}-$, $-SO_2NR^{30}-$, $-NR^{31}SO_2-$ or $-NR^{32}-$ (wherein R^{28}, R^{29}, R^{30}, R^{31} and R^{32} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) or X^5 is carbonyl, and R^{27} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl or R^{27} is C_{1-3}alkyl with the proviso that when R^{27} is C_{1-3}alkyl, X^5 is -S-, -SO-, $-SO_2-$, $-SO_2NR^{30}-$ or $-NR^{31}SO_2-$ and X^1 is not $-CH_2-$);

7) C_{1-3}alkoxyC_{2-4}alkyl provided that X^1 is -S-, -SO- or -SO_2-;

8) C_{1-3}alkoxyC_{2-4}alkyl or C_{1-4}alkyl provided that X^1 is -O-;

9) C_{1-5}alkylX^6C_{1-5}alkylR^{33} (wherein X^6 represents -O-, -S-, -SO-, -SO_2-, -NR^{34}CO-, -$CONR^{35}$-, -SO_2NR^{36}-, -$NR^{37}SO_2$- or -NR^{38}- (wherein R^{34}, R^{35}, R^{36}, R^{37} and R^{38} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{33} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

10) R^{39} (wherein R^{39} is a group selected from pyrrolidin-3-yl, piperidin-3-yl and piperidin-4-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

11) C_{1-5}alkylR^{40} (wherein R^{40} is piperazin-1-yl which bears at least one substituent selected from C_{1-4}alkanoyl, C_{1-4}alkoxycarbonyl, C_{1-4}hydroxyalkyl and -$CONR^{41}R^{42}$ (wherein R^{41} and R^{42} each independently represents hydrogen or C_{1-4}alkyl);

12) C_{1-5}alkylR^{43} (wherein R^{43} is morpholino which may bear one or two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) with the proviso that when R^4 is C_{1-5}alkylR^{43}, X^1 is -S-, -SO-, -SO_2-, -SO_2NR^9- or -$NR^{10}SO_2$-; and

13) C_{1-5}alkylR^{44} (wherein R^{44} is morpholino which bears at least one and optionally two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

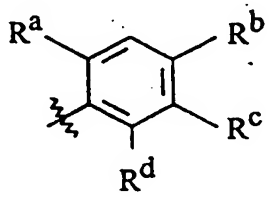
with the further proviso that when R^4 is selected from group 8) R^1 and/or R^2 is/are nitro or at least one R^3 is C_{1-3}alkanoyloxy;]

and salts thereof.

2. A quinazoline derivative as claimed in claim 1 wherein R^1 represents hydrogen, hydroxy, cyano, nitro, trifluoromethyl, methyl, ethyl, methoxy or ethoxy.

3. A quinazoline derivative as claimed in claim 1 or claim 2 wherein R^2 is hydrogen.

4. A quinazoline derivative as claimed in any one of the preceding claims wherein the phenyl group bearing $(R^3)_m$ is of the formula II:



(II)

wherein:

R^a represents hydrogen, methyl, fluoro or chloro;

R^b represents hydrogen, methyl, methoxy, bromo, fluoro or chloro;

R^c represents hydrogen or hydroxy;

R^d represents hydrogen, fluoro or chloro.

5. A quinazoline derivative as claimed in any one of the preceding claims wherein X^1 represents -O-, -S-, $-NR^7CO-$, $-NR^{10}SO_2-$ or $-NR^{11}-$ (wherein R^7, R^{10} and R^{11} each independently represents hydrogen, C_{1-2}alkyl or C_{1-2}alkoxyethyl).

6. A quinazoline derivative as claimed in any one of the preceding claims wherein R^4 is selected from one of the following eleven groups:

1) C_{1-4}alkylR^{12} (wherein R^{12} is a group selected from 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithiolan-2-yl, 1,3-dithian-2-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, morpholin-2-yl, morpholin-3-yl and piperazin-2-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-}

$_3$alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl) or C_{2-4}alkylR^{45} (wherein R^{45} is a group selected from imidazolidin-1-yl, pyrrolidin-1-yl and thiomorpholino which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl);

2) 1-R^{46}prop-1-en-3-yl, 1-R^{46}but-2-en-4-yl, 1-R^{46}but-1-en-3-yl, 1-R^{46}pent-2-en-4-yl or 2-R^{46}pent-3-en-5-yl (wherein R^{46} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to the alkenyl group through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl) or 1-R^{47}but-2-en-4-yl, 1-R^{47}pent-2-en-4-yl or 2-R^{47}pent-3-en-5-yl (wherein R^{47} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, of which one is N and the other is selected independently from O, S and N, which heterocyclic group is linked to the alkenyl group through a nitrogen atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl);

3) 1-R^{48}prop-1-yn-3-yl, 1-R^{48}but-2-yn-4-yl, 1-R^{48}but-1-yn-3-yl, 1-R^{48}pent-2-yn-4-yl or 2-R^{48}pent-3-yn-5-yl (wherein R^{48} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to the alkynyl group through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl) or 1-R^{49}but-2-yn-4-yl, 1-R^{49}pent-2-yn-4-yl or 2-R^{49}pent-3-yn-5-yl (wherein R^{49} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, of which one is N and the other is selected independently from O, S and N, which heterocyclic group is linked to the alkynyl group through a nitrogen atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-}

$_3$hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl);

4) $C_{2-3}alkylX^2C_{1-3}alkylX^3R^{16}$ (wherein X^2 and X^3 are as defined in claim 1 and R^{16} represents hydrogen or C_{1-3}alkyl) with the proviso that X^1 cannot be $-CH_2-$ when R^4 is $C_{2-3}alkylX^2C_{1-3}alkylX^3R^{16}$;

5) $C_{2-3}alkylX^4COR^{22}$ (wherein X^4 is as defined in claim 1 and R^{22} represents $-NR^{24}R^{25}$ or $-OR^{26}$ (wherein R^{24}, R^{25} and R^{26} which may be the same or different each represents hydrogen, C_{1-4}alkyl or C_{1-2}alkoxyethyl));

6) $C_{2-3}alkylX^5R^{27}$ (wherein X^5 is as defined in claim 1 and R^{27} represents a group selected from cyclopentyl, cyclohexyl, pyrrolidinyl and piperidinyl which group is linked to X^5 through a carbon atom and which group may carry one substituent selected from oxo, hydroxy, halogeno, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, C_{1-2}alkoxy, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl or R^{27} is C_{1-3}alkyl with the proviso that when R^{27} is C_{1-3}alkyl, X^5 is -S-, -SO-, $-SO_2-$, $-SO_2NR^{30}-$ or $-NR^{31}SO_2-$ and X^1 is not $-CH_2-$);

7) $C_{1-2}alkoxyC_{2-3}$alkyl provided that X^1 is -S-, -SO- or $-SO_2-$;

8) $C_{2-3}alkylX^6C_{2-3}alkylR^{33}$ (wherein X^6 is as defined in claim 1 and R^{33} represents a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl, and C_{1-3}alkoxycarbonyl);

9) $C_{2-3}alkylR^{40}$ (wherein R^{40} is piperazin-1-yl which bears at least one substituent selected from acetyl, C_{1-2}alkoxycarbonyl, C_{1-2}hydroxyalkyl and $CONR^{41}R^{42}$ (wherein R^{41} and R^{42} each independently represents hydrogen or C_{1-2}alkyl);

10) $C_{2-3}alkylR^{43}$ (wherein R^{43} is morpholino which may bear one or two substituents selected from oxo, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl) with the proviso that when R^4 is $C_{2-3}alkylR^{43}$, X^1 is -S-, -SO-, $-SO_2-$, $-SO_2NR^9-$ or $-NR^{10}SO_2-$; and

11) C_{2-3}alkylR^{44} (wherein R^{44} is morpholino which bears at least one and optionally two substituents selected from oxo, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl).

7. A quinazoline derivative as claimed in claim 6 wherein R^4 is selected from one of the following nine groups:

1) C_{1-3}alkylR^{12} (wherein R^{12} is a group selected from 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithiolan-2-yl, 1,3-dithian-2-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, morpholin-2-yl, morpholin-3-yl and piperazin-2-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, C_{1-2}alkoxy, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl) or C_{2-3}alkylR^{45} (wherein R^{45} is a group selected from imidazolidin-1-yl, pyrrolidin-1-yl and thiomorpholino which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, C_{1-2}alkoxy, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl);

2) 1-R^{50}but-2-en-4-yl (wherein R^{50} is a group selected from imidazolidin-1-yl, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithiolan-2-yl, 1,3-dithian-2-yl, piperidin-4-yl, pyrrolidin-1-yl, pyrrolidin-3-yl, piperazin-1-yl, morpholino, thiomorpholino and piperidino which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, C_{1-2}alkoxy, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl);

3) 1-R^{51}but-2-yn-4-yl (wherein R^{51} is a group selected from imidazolidin-1-yl, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithiolan-2-yl, 1,3-dithian-2-yl, piperidin-4-yl, pyrrolidin-1-yl, pyrrolidin-3-yl, piperazin-1-yl, morpholino, thiomorpholino and piperidino which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, C_{1-2}alkoxy, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl);

4) C_{2-3}alkylX^2C_{1-3}alkylX^3R^{16} (wherein X^2 and X^3 are as defined in claim 1 and R^{16} represents hydrogen or C_{1-3}alkyl) with the proviso that X^1 cannot be $-CH_2-$ when R^4 is C_{2-3}alkylX^2C_{1-3}alkylX^3R^{16};

5) C_{1-2}alkoxyC_{2-3}alkyl provided that X^1 is -S-, -SO- or -SO_2-;

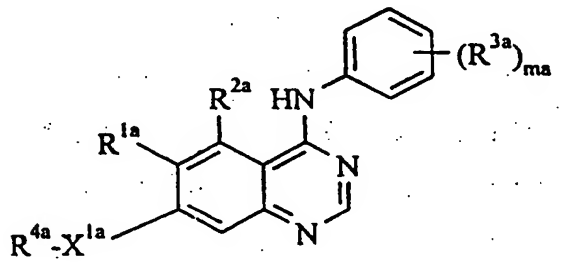
6) 2-(3,3-dimethylureido)ethyl, 3-(3,3-dimethylureido)propyl, 2-(3-methylureido)ethyl, 3-(3-methylureido)propyl, 2-ureidoethyl, 3-ureidopropyl, 2-(N,N-dimethylcarbamoyloxy)ethyl, 3-(N,N-dimethylcarbamoyloxy)propyl, 2-(N-methylcarbamoyloxy)ethyl, 3-(N-methylcarbamoyloxy)propyl, 2-(carbamoyloxy)ethyl, 3-(carbamoyloxy)propyl, 2-(1,3,3-trimethylureido)ethyl, 3-(1,3,3-trimethylureido)propyl, 2-(isopropoxycarbonylamino)ethyl, 3-(isopropoxycarbonylamino)propyl, 2-(isobutoxycarbonylamino)ethyl, 3-(isobutoxycarbonylamino)propyl, 2-(t-butoxycarbonylamino)ethyl or 3-(t-butoxycarbonylamino)propyl;

7) C_{2-3}alkylX^5R^{27} (wherein R^{27} is C_{1-2}alkyl and X^5 is -S-, -SO-, -SO_2-, -SO_2NR^{30}- or -$NR^{31}SO_2$- and with the proviso that X^1 is not -CH_2-);

8) C_{2-3}alkylX^6C_{2-3}alkylR^{33} (wherein X^6 is as defined in claim 1 and R^{33} represents a group selected from morpholino, 2-oxopyrrolidin-1-yl, pyrrolidin-1-yl, piperidino, piperazin-1-yl and 4-methylpiperazin-1-yl); and

9) C_{2-3}alkylR^{43} (wherein R^{43} is morpholino which may bear one or two substituents selected from oxo, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl) with the proviso that when R^4 is C_{2-3}alkylR^{43}, X^1 is -S-, -SO-, -SO_2-, -SO_2NR^9- or -$NR^{10}SO_2$-.

8. A compound as claimed in claim 1 of the formula Ia:



(Ia)

[wherein:

R^{1a} is hydrogen or methoxy;

R^{2a} is hydrogen;

the phenyl group bearing $(R^{3a})_{ma}$ is the 4-chloro-2-fluorophenyl group or the 4-bromo-2-fluorophenyl group;

X^{1a} is -O-, -S-, -$NR^{5a}CO$- or -$NR^{6a}SO_2$- (wherein R^{5a} and R^{6a} each independently represents hydrogen or C_{1-2}alkyl);

R^{4a} is selected from one of the following eleven groups:

1) C_{1-4}alkylR^{7a} (wherein R^{7a} is a group selected from 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithiolan-2-yl, 1,3-dithian-2-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, morpholin-2-yl, morpholin-3-yl and piperazin-2-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl) or C_{2-4}alkylR^{8a} (wherein R^{8a} is a group selected from imidazolidin-1-yl, pyrrolidin-1-yl and thiomorpholino which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl);

2) 1-R^{9a}prop-1-en-3-yl, 1-R^{9a}but-2-en-4-yl, 1-R^{9a}but-1-en-3-yl, 1-R^{9a}pent-2-en-4-yl or 2-R^{9a}pent-3-en-5-yl (wherein R^{9a} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to the alkenyl group through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl) or 1-R^{10a}but-2-en-4-yl, 1-R^{10a}pent-2-en-4-yl or 2-R^{10a}pent-3-en-5-yl (wherein R^{10a} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, of which one is N and the other is selected independently from O, S and N, which heterocyclic group is linked to the alkenyl group through a nitrogen atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl);

3) 1-R^{11a}prop-1-yn-3-yl, 1-R^{11a}but-2-yn-4-yl, 1-R^{11a}but-1-yn-3-yl, 1-R^{11a}pent-2-yn-4-yl or 2-R^{11a}pent-3-yn-5-yl (wherein R^{11a} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to the alkynyl group through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl) or 1-R^{12a}but-2-yn-4-yl, 1-R^{12a}pent-2-yn-4-yl or 2-R^{12a}pent-3-yn-5-yl (wherein R^{12a} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, of which one is N and the other is selected independently from O, S and N, which heterocyclic group is linked to the alkynyl group through a nitrogen atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl and C_{1-3}alkoxycarbonyl);

4) C_{2-3}alkyl$X^{2a}C_{1-3}$alkyl$X^{3a}R^{13a}$ (wherein X^{2a} and X^{3a} which may be the same or different each represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{14a}CO-$, or $-NR^{15a}-$ (wherein R^{14a} and R^{15a} each independently represents hydrogen, C_{1-2}alkyl or C_{1-2}alkoxyethyl) and R^{13a} represents hydrogen or C_{1-3}alkyl);

5) C_{2-3}alkyl$X^{4a}COR^{16a}$ (wherein X^{4a} represents -O- or $-NR^{17a}-$ (wherein R^{17a} represents hydrogen, C_{1-3}alkyl or C_{1-2}alkoxyethyl) and R^{16a} represents $-NR^{18a}R^{19a}$ or $-OR^{20a}$ (wherein R^{18a}, R^{19a} and R^{20a} which may be the same or different each represents hydrogen, C_{1-4}alkyl or C_{1-2}alkoxyethyl));

6) C_{2-3}alkyl$X^{5a}R^{21a}$ (wherein X^{5a} represents carbonyl, -O-, -S-, -SO-, $-SO_2-$, $-NR^{22a}CO-$, $-NR^{23a}SO_2-$ or $-NR^{24a}-$ (wherein R^{22a}, R^{23a} and R^{24a} each independently represents hydrogen, C_{1-2}alkyl or C_{1-2}alkoxyethyl) and R^{21a} represents a group selected from cyclopentyl, cyclohexyl, pyrrolidinyl and piperidinyl which group is linked to X^{5a} through a carbon atom and which group may carry one substituent selected from oxo, hydroxy, halogeno, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, C_{1-2}alkoxy, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl or R^{21a} is C_{1-3}alkyl with the proviso that when R^{21a} is C_{1-3}alkyl, X^{5a} is -S-, -SO-, $-SO_2-$ or $-NR^{23a}SO_2-$);

7) C_{1-2}alkoxyC_{2-3}alkyl provided that X^{1a} is -S-;

8) C_{2-3}alkyl$X^{6a}C_{2-3}$alkylR^{25a} (wherein X^{6a} represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{26a}CO-$, $-NR^{27a}SO_2-$ or $-NR^{28a}-$ (wherein R^{26a}, R^{27a} and R^{28a} each independently represents hydrogen, C_{1-2}alkyl or C_{1-2}alkoxyethyl) and R^{25a} represents a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, carbamoyl, C_{1-3}alkylcarbamoyl, N,N-di(C_{1-3}alkyl)carbamoyl, C_{2-3}alkanoyl, and C_{1-3}alkoxycarbonyl);

9) C_{2-3}alkylR^{29a} (wherein R^{29a} is piperazin-1-yl which bears at least one substituent selected from acetyl, C_{1-2}alkoxycarbonyl, C_{1-2}hydroxyalkyl and $CONR^{30a}R^{31a}$ (wherein R^{30a} and R^{31a} each independently represents hydrogen or C_{1-2}alkyl);

10) C_{2-3}alkylR^{32a} (wherein R^{32a} is morpholino which may bear one or two substituents selected from oxo, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl) with the proviso that when R^{4a} is C_{2-3}alkylR^{32a}, X^{1a} is -S- or $-NR^{6a}SO_2-$ (wherein R^{6a} is as defined herein); and

11) C_{2-3}alkylR^{33a} (wherein R^{33a} is morpholino which bears at least one and optionally two substituents selected from oxo, C_{1-2}alkyl, C_{1-2}hydroxyalkyl, carbamoyl, C_{1-2}alkylcarbamoyl, N,N-di(C_{1-2}alkyl)carbamoyl, acetyl and C_{1-2}alkoxycarbonyl);]

and salts thereof.

9. A quinazoline derivative as claimed in claim 1 selected from:-

4-(4-chloro-2-fluoroanilino)-7-(1,3-dioxolan-2-ylmethoxy)-6-methoxyquinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(4-morpholinobut-2-yn-1-yloxy)quinazoline,

(E)-4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(4-morpholinobut-2-en-1-yloxy)quinazoline,

4-(4-chloro-2-fluoroanilino)-7-(3-(2,6-dimethylmorpholino)propoxy)-6-methoxyquinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(3-([N-methyl-N-methylsulphonyl]amino)propoxy)quinazoline,

7-(2-[N-tert-butoxycarbonylamino]ethoxy)-4-(4-chloro-2-fluoroanilino)-6-methoxyquinazoline,

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(3-([N-methyl-N-methylsulphonyl]amino)propoxy)quinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-(2-oxoimidazolidin-1-yl)ethoxy)quinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-(3-oxomorpholino)ethoxy)quinazoline,

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(2-(3-oxomorpholino)ethoxy)quinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-thiomorpholinoethoxy)quinazoline,

(S)-4-(4-bromo-2-fluoroanilino)-7-(3-(2-carbamoylpyrrolidin-1-yl)propoxy)-6-methoxyquinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(3-(2-oxopyrrolidin-1-yl)propoxy)quinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-(2-oxopyrrolidin-1-yl)ethoxy)quinazoline,

(S)-7-(3-(2-carbamoylpyrrolidin-1-yl)propoxy)-4-(4-chloro-2-fluoroanilino)-6-methoxyquinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-(2-morpholinoethoxy)ethoxy)quinazoline and

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(3-(2-oxopyrrolidin-1-yl)propoxy)quinazoline

and salts thereof.

10. A quinazoline derivative as claimed in claim 1 selected from:-

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-2-(2-methoxyethoxy)ethoxyquinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-3-yl)methoxyquinazoline,

4-(4-bromo-2-fluoroanilino)-7-(3-(1,1-dioxothiomorpholino)propoxy)-6-methoxyquinazoline,

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(2-(2-methoxyethoxy)ethoxy)quinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-(2-pyrrolidin-1-ylethoxy)ethoxy)quinazoline,
4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-(2-[4-methylpiperazin-1-yl]ethoxy)ethoxy)quinazoline,
4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(3-morpholinopropylthio)quinazoline,
4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(2-([N-methyl-N-methoxyacetyl]amino)ethoxy)quinazoline and
4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(2-(2-oxopyrrolidin-1-yl)ethoxy)quinazoline
and salts thereof.

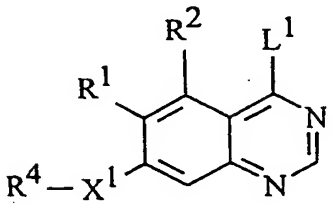
11. A quinazoline derivative as claimed in claim 1 selected from:-
(E)-4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(4-(pyrrolidin-1-yl)but-2-en-1-yloxy)quinazoline,
4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(3-(methylsulphonyl)propoxy)quinazoline,
(S)-4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-3-yl)methoxyquinazoline and
(R)-4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-3-yl)methoxyquinazoline
and salts thereof.

12. A quinazoline derivative as claimed in claim 1 selected from:-
4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(3-(methylsulphonyl)propoxy)quinazoline
and salts thereof.

13. A quinazoline derivative as claimed in any one of the preceding claims in the form of a pharmaceutically acceptable salt.

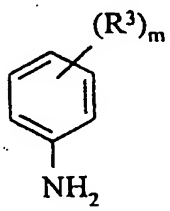
14. A process for the preparation of a quinazoline derivative of formula I or salt thereof (as defined in claim 1) which comprises:-

(a) the reaction of a compound of the formula III:



(III)

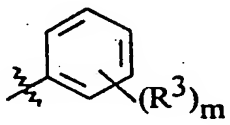
(wherein R^1, R^2, X^1 and R^4 are as defined in claim 1 and L^1 is a displaceable moiety), with a compound of the formula IV:



(IV)

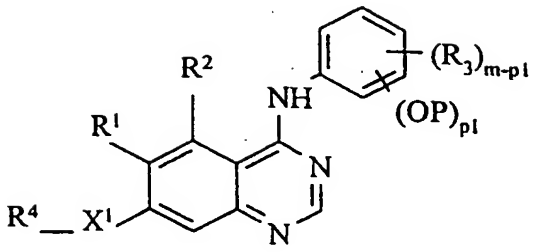
(wherein R^3 and m are as defined in claim 1) whereby to obtain compounds of the formula I and salts thereof;

(b) for the preparation of compounds of formula I and salts thereof in which the group of formula IIa:



(IIa)

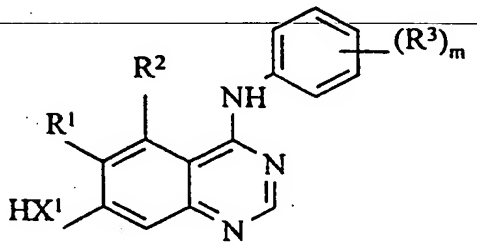
(wherein R^3 and m are as defined in claim 1) represents a phenyl group carrying one or more hydroxy groups, the deprotection of a compound of formula V:



(V)

(wherein X^1, m, R^1, R^2, R^3 and R^4 are as defined in claim 1, P represents a phenolic hydroxy protecting group and p1 is an integer from 1 to 5 equal to the number of protected hydroxy groups and such that m-p1 is equal to the number of R^3 substituents which are not protected hydroxy);

(c) for the preparation of those compounds of formula I and salts thereof wherein the substituent X^1 is -O-, -S-, $-NR^{11}$-, $-SO_2$-, $-CONR^8$- or $-SO_2NR^9$-, the reaction of a compound of the formula VI:



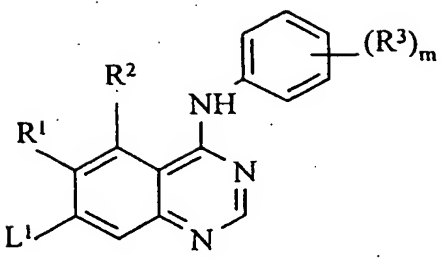
(VI)

(wherein m, X^1, R^1, R^2 and R^3 are as defined in claim 1) with a compound of formula VII:

$$R^4\text{-}L^1 \qquad \text{(VII)}$$

(wherein R^4 is as defined in claim 1 and L^1 is as defined herein);

(d) the reaction of a compound of the formula VIII:



(VIII)

with a compound of the formula IX:

$$R^4\text{-}X^1\text{-}H \qquad (IX)$$

(wherein R^1, R^2, R^3, R^4, m and X^1 are as defined in claim 1 and L^1 is as defined herein);

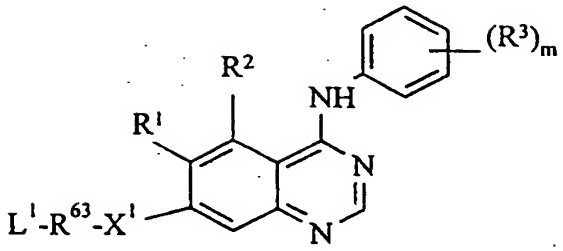
(e) for the preparation of compounds of formula I and salts thereof wherein R^4 is $C_{1-5}alkylR^{53}$, [wherein R^{53} is selected from one of the following three groups:

1) X^7R^{27} (wherein X^7 represents -O-, -S-, $-SO_2-$, $-NR^{54}CO-$, $-NR^{55}SO_2-$ or $-NR^{56}-$ (wherein R^{54}, R^{55} and R^{56} each independently represents hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$) and R^{27} is as defined in claim 1);

2) $X^8C_{1-5}alkylX^3R^{16}$ (wherein X^8 represents -O-, -S-, $-SO_2-$, $-NR^{57}CO-$, $-NR^{58}SO_2-$ or $-NR^{59}-$ (wherein R^{57}, R^{58} and R^{59} each independently represents hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$) and X^3 and R^{16} are as defined in claim 1); and

3) $X^9C_{1-5}alkylR^{33}$ (wherein X^9 represents -O-, -S-, $-SO_2-$, $-NR^{60}CO-$, $-NR^{61}SO_2-$ or $-NR^{62}-$ (wherein R^{60}, R^{61} and R^{62} each independently represents hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$) and R^{33} is as defined in claim 1);],

the reaction of a compound of the formula X:



(X)

(wherein X^1, R^1, R^2, R^3 and m are as defined in claim 1, L^1 is as defined herein and R^{63} is C_{1-5}alkyl) with a compound of the formula XI:

$$R^{53}\text{-}H \qquad \text{(XI)}$$

(wherein R^{53} is as defined herein) to give a compound of the formula I;
the preparation of compounds of the formula I wherein R^4 is C_{2-5}alkylR^{45}, (wherein R^{45} is a group selected from imidazolidin-1-yl, pyrrolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl), the reaction of a compound of formula X (wherein R^{63} is C_{2-5}alkyl) with a compound of the formula XIa:

$$R^{45}\text{-}H \qquad \text{(XIa)}$$

(wherein R^{45} is as defined herein) to give a compound of the formula I;

(f) for the preparation of those compounds of the formula I and salts thereof wherein the substituent R^1 is represented by $-NR^5R^6$, where one or both of R^5 and R^6 are C_{1-3}alkyl, the reaction of compounds of formula I wherein the substituent R^1 is an amino group with an alkylating agent;

(g) for the preparation of compounds of formula I and salts thereof wherein one or more of the substituents R^1, R^2 or R^3 is an amino group, the reduction of a

corresponding compound of formula I wherein the substituent(s) at the corresponding position(s) of the quinazoline and/or aniline ring is/are a nitro group(s);
and when a pharmaceutically acceptable salt of a quinazoline derivative of formula I is required, reaction of the compound obtained with an acid or base whereby to obtain the desired pharmaceutically acceptable salt.

15. A pharmaceutical composition which comprises as active ingredient a compound of formula I as defined in claim 1 or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable excipient or carrier.

16. A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof as defined in claim 1.